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Varicella hospitalizations in Los Angeles during the varicella vaccination era, 2003–2011: Are they preventable?

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Abstract

Characteristics of varicella-related hospitalizations in the mature varicella vaccination era, including the proportion vaccinated and the severity of disease, are not well described. We present the vaccination status, severity and reasons for hospitalization of the hospitalized varicella cases reported to the Los Angeles County Health Department from 2003 to 2011, the period which includes the last 4 years of the mature one-dose program and the first 5 years after introduction of the routine two-dose program. A total of 158 hospitalized varicella cases were reported overall, of which 52.5% were potentially preventable and eligible for vaccination, 41.8% were not eligible for vaccination, and 5.7% were vaccinated. Most hospitalizations (72.2%) occurred among healthy persons, 54.4% occurred among persons ≥20 years of age, and 3.8% of hospitalizations resulted in death. Our data suggest that as many as half of the hospitalized varicella cases, including half of the deaths, may have been preventable given that they occurred in persons who were eligible for vaccination. More complete implementation of the routine varicella vaccination program could further reduce the disease burden of severe varicella.

Keywords

Varicella hospitalizations; Varicella vaccination; Varicella complications; Severe varicella

1. Introduction

Although often a mild disease of childhood, varicella can result in serious morbidity and mortality. Increasing age and chronic co-morbid conditions have been identified as risk factors for severe varicella [1–4]; however, before introduction of the varicella vaccine in 1995, over half of varicella hospitalizations were in previously healthy children less than 15 years of age [1]. Following the one-dose varicella vaccine recommendation for children by

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the Advisory Committee on Immunization Practices (ACIP) in 1996 [5], the number of hospitalizations due to varicella declined 67%, with the majority of hospitalizations still occurring among previously healthy persons [2,6–10]. In 2001, California implemented a one-dose school entry requirement for varicella vaccine that is now required for all students entering grades K-12. In 2006, a routine two-dose varicella vaccination program was implemented in the United States to further reduce varicella disease and its complications [11].

Declines in the number of varicella-related hospitalizations during the early years of the two-dose varicella vaccination program have been documented [12]. However, characteristics of varicella-related hospitalizations in the mature varicella vaccination era, including the proportion vaccinated and the severity of disease, are not well described. This study describes the vaccination status, severity, and reasons for hospitalization for varicella hospitalizations among cases reported to the Los Angeles County Health Department from 2003 to 2011, a period that includes the last 4 years of the mature one-dose program and the first 5 years after introduction of the routine two-dose program. Understanding the characteristics of cases requiring hospitalization will help inform strategies for further reducing severe disease.

2. Methods

The Los Angeles County Department of Public Health (LACDPH) has collected information on cases of hospitalized varicella in Los Angeles County since it was added to the California Code of Regulations as a reportable condition in 2003. The study population included all hospitalized varicella cases residing in Los Angeles County reported to the LACDPH with disease onset between January 1, 2003 and December 31, 2011. As part of mandated public health investigations, data on patient demographics, medical history, vaccination history, and clinical course were abstracted by health department staff from hospital records for each case.

2.1. Definitions

A probable case of varicella was defined as an acute illness with diffuse (generalized) maculopapulovesicular rash without laboratory confirmation or an epidemiologic linkage to another probable or confirmed case [13]. A confirmed case of varicella was defined as an acute illness with diffuse (generalized) maculopapulovesicular rash and either laboratory confirmation of varicella or epidemiologic linkage to another probable or confirmed case [13]. A varicella-related hospitalization was defined as a probable or confirmed case of varicella that was hospitalized for at least 24 h.

Cases were categorized as being hospitalized for precautionary reasons if they had a chronic condition that resulted in the hospitalization without which they would otherwise not be hospitalized. Cases were categorized as hospitalized for varicella if they had severe varicella-related symptoms, such as fever or profuse rash, which required hospitalization. Cases were categorized as hospitalized for varicella-related complications if the disease resulted in a complication which required hospitalization.

Reported varicella-related complications were categorized as: pulmonary (including pneumonia, respiratory failure, bronchiolitis), dermatologic (including secondary skin infections, cellulitis, impetigo), bacteremia/sepsis, dehydration, and neurologic (including encephalitis, cerebellar ataxia, meningitis, altered level of consciousness, seizures). Cases could have multiple complications.

Chronic conditions were health conditions present before hospitalization and were categorized as: immunocompromised (including cancer, HIV/AIDS, previous organ transplant, autoimmune disorder), chronic renal failure, chronic lung disease, diabetes, and asthma. Cases could have multiple chronic conditions.

Cases were categorized as vaccinated if they had documented proof (e.g., immunization record) of previous vaccination with at least one dose of varicella-containing vaccine. Cases were considered as breakthrough varicella if they developed varicella 42 or more days after vaccination. Cases were classified as potentially preventable if they did not fall into one of the following categories: had documented proof of previous varicella disease, had been vaccinated with at least one dose of varicella-containing vaccine, or were immunocompromised. Cases in pregnant women were considered as potentially preventable if they had not been previously vaccinated with at least one dose of varicella-containing vaccine before pregnancy.

2.2. Data analysis

Data were analyzed using SAS 9.2 software (SAS Institute Inc., Cary, NC). Poisson regression analysis was used to compare overall hospitalization rates and rates by age group between the mature one-dose (2003–2006) and the early two-dose (2007–2011) varicella vaccination eras.

3. Results

A total of 369 suspected cases of varicella that required hospitalization were reported in Los Angeles County with disease onset between 2003 and 2011. After excluding 39 (10.6%) that were determined to be herpes zoster and 172 (46.6%) determined not to be varicella, 158 (42.8%) varicella hospitalizations were included in the analysis. Sixty-nine of the hospitalized varicella cases were reported during 2003–2006 and 89 during 2007–2011, after implementation of the routine two-dose varicella vaccine program era, with a rate of 0.2 hospitalized varicella cases/100,000 population during each era, 2003–2006 and 2007–2011 ($p = 0.9$). No statistically significant differences between hospitalization rates by vaccination program era were identified for any of the age groups (data not shown). Demographic and hospitalization characteristics of the cases are presented in Table 1. The median number of days hospitalized was 5 (range 1–174). Just over half (54.4%) of the hospitalized cases were ≥20 years of age; 16 (10.1%) were pregnant. Most hospitalizations (72.2%) occurred among healthy persons. Twenty-seven (17.1%) hospitalized varicella cases whose country of birth was known were born outside of the United States: 15 in Asia and 12 in Central/South America. Of these foreign-born cases, 5 (18.5%) were pregnant and 12 (44.4%) had chronic conditions prior to hospitalization. Nine (5.7%) hospitalized varicella cases had documentation of at least one dose of varicella vaccination. Six (3.8%) case-patients died.

Data on vaccination status and place of birth were missing for 52% of cases while 48% of cases were missing information on laboratory confirmation. Less than 5% of cases were missing data on race/ethnicity or chronic health conditions.

3.1. Potentially preventable hospitalizations

Of the 83 (52.5%) hospitalized varicella cases that were potentially preventable, 23 (27.7%) were 1–19 years of age, and 60 (72.3%) were ≥20 years of age. Twenty-seven (32.5%) of the potentially preventable cases were laboratory confirmed. Of those whose country of birth was known, 21 were born in the United States, 3 in Mexico, 12 in Asia, and 6 in Central/South America. Twenty-three (27.7%) were admitted for precautionary reasons, of which 15 (65.2%) were pregnant; 56 (67.5%) were admitted for varicella or varicella-related complications; and 4 (4.8%) for other medical conditions (i.e., atrial fibrillation, heart surgery, alcohol withdrawal, shunt infection) who were incubating disease upon admission. Thirty-five (42.2%) of the hospitalized varicella cases that were potentially preventable experienced at least one varicella complication, including pulmonary (15), neurologic (5), and dermatologic (5) complications, bacteremia (3) and dehydration (3). Three of the potentially preventable hospitalizations resulted in death; one occurred in a 1 year old child who was scheduled for vaccination and experienced bacteremia and dehydration and 2 were ≥20 years of age.

3.2. Hospitalizations among persons not eligible for vaccination

A total of 66 (41.8%) varicella cases among persons not eligible for vaccination were hospitalized, including 25 (37.9%) who were <1 year of age (14 were <6 months and 11 were 6–11 months of age) and 41 (62.1%) who were immunocompromised. Twenty-two (33.3%) of the cases ineligible for vaccination were laboratory confirmed. Reasons for admission among the cases that were not eligible for vaccination included: 28 (42.4%) for varicella or varicella-related complications, including 6 infants <6 months and 8 infants 6–11 months of age; 37 (56.1%) for precautionary reasons, including 8 infants <6 months and 3 infants 6–11 months of age; and 1 (1.5%) that developed varicella while hospitalized for a liver transplant. Thirty-one (47.0%) of the cases not eligible for vaccination developed at least one complication, including dermatologic (12), pulmonary (10), and neurologic (4) complications, bacteremia (3), and dehydration (1). Three of the hospitalizations that occurred among persons not eligible for vaccination resulted in death; all were ≥20 years of age and immunocompromised.

3.3. Hospitalizations among vaccinated persons

Nine (5.7%) of the hospitalized varicella cases had been vaccinated against varicella; one (11.1%) was laboratory confirmed. All were children, of whom two were 1–4 years of age and seven were 11–14 years of age. Seven (77.8%) of the cases had received one dose and 2 (22.2%) had received two doses of varicella-containing vaccine. Seven of the cases were considered breakthrough varicella and two developed a rash within 42 days of vaccination. Four of the vaccinated cases were immunocompromised; each had received one dose of varicella-containing vaccine. Five (71.4%) of the vaccinated cases that had received one dose were hospitalized for precautionary reasons and 2 (28.6%) for varicella or varicella-related complications. The two case-patients that had received two doses of varicella-

containing vaccine were admitted for cellulitis. None of the hospitalized vaccinated cases resulted in death.

4. Discussion

While varicella is often a self-limiting disease, it can be severe, requiring hospitalization and resulting in death. Varicella-related hospitalizations decreased by 65% in all age groups during the one-dose varicella vaccination era and additional declines have been reported since implementation of the two-dose program [12,14]. Our descriptive data on hospitalized cases of varicella in Los Angeles County demonstrate that, as in the prevaccination era, most hospitalized cases of varicella continue to occur among previously healthy persons with no immunocompromising conditions. Although the population under surveillance in our study may have been too small to detect differences in the rate of hospitalization between the mature one-dose and early two-dose varicella vaccination program eras, our data suggest that as many as half of hospitalized varicella cases, including half of the deaths, may have been preventable given that they occurred in persons who were eligible for vaccination. More complete implementation of the routine varicella vaccination program could further reduce the disease burden of severe varicella.

Varicella-related hospitalizations declined in all age groups during the one-dose era including among 0–4 year olds suggesting a benefit of the vaccination program among those too young to be fully vaccinated [2,6–9,12]. We did not document a decline in infant hospitalization rates in our study but it appeared that younger infants were more often hospitalized for precautionary reasons compared with older infants who were more likely to be hospitalized for severe disease. However, this difference was not statistically significant. Younger infants may benefit from protection provided by maternal antibodies, which start to wane after the first few months of life, and therefore may experience less severe disease compared with older infants [15]. Hospitalizations among infants continue to occur in the varicella vaccination era and these findings highlight the importance of vaccinating close contacts of individuals unable to receive varicella vaccine due to age or contraindication [11].

We identified a small number of varicella cases that resulted in hospitalization among children who had received varicella vaccine. Half of these cases were in children with immunocompromising conditions, none of whom had received two doses. An estimated 15–20% of children may not respond to a single dose of varicella vaccine [16]. Whether these hospitalizations could have been prevented had these children received two doses of varicella vaccine prior to becoming immunocompromised is not known, but it highlights the importance of receiving vaccinations on schedule. Three of the hospitalized varicella cases among previously healthy children that were vaccinated, including the two who had received two doses, appeared to be severe. While the data to date indicate that severe breakthrough varicella is rare, ongoing monitoring of varicella hospitalizations will be important for providing a better understanding of the potential for severe breakthrough varicella.

Although declines of varicella hospitalizations among adults have been demonstrated during the early two-dose varicella vaccination era [12], rates of hospitalizations among adults in

Los Angeles County did not change over time (data not shown). Many of the adult hospitalized cases in Los Angeles County were admitted for precautionary reasons, including several that were pregnant. These cases highlight the importance of high vaccination coverage and catch-up vaccination to ensure that adolescents and adults are protected as varicella can be more severe in adulthood and during pregnancy. Prenatal assessment of women for evidence of varicella immunity is recommended with vaccination of susceptible individuals prior to or upon completion of pregnancy [11]. Additionally, several of the hospitalized cases among adults were in persons who were foreign-born. It is important for clinicians to remember that the epidemiology of varicella is different in tropical countries and foreign-born adults should not be assumed to be protected against varicella [17].

There were limitations to our study. A majority of the potentially preventable hospitalizations that we identified occurred in persons ≥20 years of age. However, due to challenges of diagnosis of varicella in adults, particularly those ≥50 years of age in whom it can be difficult to clinically distinguish herpes zoster from varicella, the total number of hospitalized cases and those that were potentially preventable may be an overestimate. Data on severity of varicella, based on lesion count, and indications for hospitalization were not systematically documented in the medical charts and thus were not available for all cases. Furthermore, more than 50% of cases were missing information on vaccination status which may have led to an underestimation of the number of hospitalizations among vaccinated persons.

Given that many hospitalizations in the mature varicella vaccination program appear to be precautionary, it will be important to consider changes in clinical management and indications for hospitalization as varicella becomes less common since this may confound use of hospitalization data to track severe varicella disease going forward. We found that more than half of the varicella hospitalizations in Los Angeles County during the varicella vaccination era, 2003–2011, were potentially preventable with vaccination. Moreover, more than half occurred among adults, suggesting that additional efforts are needed to identify and target susceptible adolescents and adults for varicella vaccination. Our study identified few hospitalizations among vaccinated persons but additional years of data are needed to determine the impact of the two-dose varicella vaccination program on varicella hospitalizations. More complete implementation of the routine varicella vaccination program could further reduce the disease burden of severe varicella.

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Table 1

Demographic and clinical characteristics of reported hospitalized varicella cases, Los Angeles County, 2003–2011, $n = 158$.

Characteristics	Potentially preventable hospitalizations ($N = 83$) n (%)	Hospitalizations in persons not eligible for vaccination ($N = 66$) n (%)	Hospitalizations in vaccinated persons[a] ($N = 9$) n (%)
Gender			
Male	42 (50.6)	40 (60.6)	7 (77.8)
Female	41 (49.4)	26 (39.4)	2 (22.2)
Age			
<1	0	25 (37.9)	0
1–4	7 (8.4)	4 (6.1)	2 (22.2)
5–9	4 (4.8)	2 (3.0)	5 (55.6)
10–14	4 (4.8)	6 (9.1)	2 (22.2)
15–19	8 (9.6)	3 (4.5)	0
20–49	48 (57.8)	14 (21.2)	0
50+	12 (14.5)	12 (18.2)	0
Race/ethnicity[a]			
Hispanic	37 (44.6)	39 (59.1)	5 (55.6)
White	22 (26.5)	7 (10.6)	0
Asian/Pacific Islander	14 (16.9)	9 (13.6)	2 (22.2)
African American/Black	7 (8.4)	8 (12.1)	1 (11.1)
Unknown	3 (3.6)	3 (4.5)	1 (11.1)
Reasons for admission			
Precautionary	23 (27.7)	37 (56.1)	5 (55.6)
Varicella-related complications	31 (37.3)	19 (28.8)	2 (22.2)
Varicella	25 (30.1)	9 (13.6)	1 (11.1)
Other	4 (4.8)	1 (1.5)	1 (11.1)
Varicella-related complications			
Yes	35 (42.2)	30 (45.4)	4 (44.4)
No	48 (57.8)	36 (54.5)	5 (55.6)
Laboratory confirmation			
Yes	27 (32.5)	22 (33.3)	1 (11.1)
No	17 (20.5)	13 (19.7)	3 (33.3)
Unknown	39 (47.0)	31 (47.0)	5 (55.6)
Died			
Yes	3 (3.6)	3 (4.5)	0
No	80 (96.4)	63 (95.5)	9 (100)

[a]Data for vaccination status and race/ethnicity were missing for 51.3% and 4.4% of cases, respectively.